



# UNITED STATES PATENT AND TRADEMARK OFFICE

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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/589,777      | 06/08/2000  | Vikas P. Sukhatme    | 1440.1023-011       | 1530             |

29933 7590 07/02/2003

PALMER & DODGE, LLP  
KATHLEEN M. WILLIAMS  
111 HUNTINGTON AVENUE  
BOSTON, MA 02199

EXAMINER

YU, MISOOK

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1642

DATE MAILED: 07/02/2003

26

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/589,777

Applicant(s)

SUKHATME, VIKAS P.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 February 2003 and 25 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-35 is/are pending in the application.
- 4a) Of the above claim(s) 5-10 and 17-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-4, 11-16 and 35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Seq. alignment*.

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The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Misook Yu.

## **DETAILED ACTION**

### ***Continued Prosecution Application***

The request filed on 2-19-2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09589777 is acceptable and a CPA has been established. An action on the CPA follows.

### ***Election/Restrictions***

Claims 2-35 are pending and claims 17-34 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8. Applicant states that claims 2-4, 11-16, and 35 are pending at page 2 of the Amendment (Paper No. 17) filed on 9-18-2002 but the review of the prosecution history indicates that claims 2-35 are still pending. If applicant wishes to cancel the claims drawn to the non-elected inventions, applicant is requested to instruct the Office explicitly (for example, by saying "cancel claims 17-34") to cancel those claims.

### ***Claim Rejections - 35 USC § 112***

Claim 35 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

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which it pertains, or with which it is most nearly connected, to make and/or use the invention. The new limitation "anti-angiogenic activity" does not obviate the rejection although the previous Office action states that the rejection may be overcome by reciting function the claimed product possesses because claim 35 recites broadly "mutant, derivative, analog or homolog of EM 1" and specification does not teach what the structure of EM1 could be changed to become "mutant, derivative, analog or homolog to EM1" and the resulting structure would still retain the recited function. Applicant argument at pages 6-12 in Paper No. 11 have been fully considered but the Office maintains this rejection because the art recognizes that protein chemistry is unpredictable as stated in Paper 9. Note also page 9 line 4 of the instant specification which says that the activity of the deletion mutant is unexpected.

### ***Allowable Subject Matter***

The indicated allowability of claims 2-4, and 11-16 is withdrawn in view of the rejections below.

## **NEW GROUNDS OF REJECTIONS**

### ***Specification***

The disclosure is objected to because it for example at page 20, contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

***Claim Rejections - 35 USC § 112***

Claims 2-4, and 11-16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is confusing for several reasons. First, the specification at page 4 line 19 says that EM1 **comprises** (note the open language, i.e., any protein that has the required sequence plus something else) amino acid sequence through amino acid 175 in Fig. 2; based on this definition, the protein sequence shown in Fig. 2 is within metes and bounds of EM1 because the protein in the instant Fig. 2 has the required sequence plus something else. Note also page 9 line 29 of the specification that says EM1 protein is SEQ ID NO:2. Second, it is not clear whether "endostatin protein" in line and "the endostatin protein" in lines 2-3 are same or not. If not, then "the endostatin protein" in lines 2-3 lacks an antecedent base in the claim. The claim as written is not clear about what is being deleted, what is a mutated endostatin protein, and what constitutes EM1. Does EM1 comprise amino acid number 1 through 175 of the protein shown in Fig.2? If the mutated endostatin protein (the protein up to amino acid number 175 of SEQ ID NO:2) is a deletion mutant, then the instant SEQ ID NO:2 comprising (open language) the deleted mutant is also EM 1. Since applicant's discovery is a deletion mutant, the open language "comprising" a mutant makes the endostatin taught by O'Reilly et al (see the art rejections below) belong to be within the scope of the claimed invention. This rejection affects all dependent claims. Overall the property boundary of claim 2 is really confusing.

Claim 2 recites the limitation "the mutation" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 11 is confusing because it is not clear whether all of the protein molecules are present as single polypeptide as a fusion protein. This rejection affects all dependent claims.

Claims 2-5, 11-16, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is based on the Office's interpretation that the claims are drawn to a genus of protein called EM1. The entire specification is about isolating an unusual mouse splicing variant consisting of amino acid 1-175 of SEQ ID NO:2, wherein said variant lacks SEQ ID NO:25 (the last 9 amino acids from the C-terminus of a protein known in the art as endostatin, wherein said variant has the surprising ability to inhibit angiogenesis despite lacking the nine consecutive amino acids at the C-terminus of endostatin. The specification in the paragraph bridging pages 9 and 10 says that EM1 encompasses proteins from any mammal. The specification teaches a species, i.e., from mouse. The specification does not teach what the structure of EM1, from other mammalian species such as one from a dog or cat, looks like. Based on one species, one cannot predict the types of additional species. Since the genus includes a large number of unpredictable species (the entire

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mammalian species), possession of only one species is not seen as sufficient to reasonably convey possession of the entire genus.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 2-4, 11, and 13-15 are rejected under 35 U.S.C. **102(a)** as being anticipated by O'Reilly et al (IDS AR, Cell, Vol 88, 277-285, 24 January 1997) as evidenced by Oh et al (1994, a copy provided with the previous Office action, Paper No. 9, Proc. Natl. Sci. Acad. USA., vol. 91, pages 4229-33) for the C-terminal 20 kDa fragment sequence information of the collagen type XVIII.

This rejection is based on the Office's interpretation that the limitation "comprising" in line 1 of claim 2 controls the scope of the claimed invention. The claims as written read on the recombinant endostatin fusion protein of O'Reilly et al. Note Expression and Purification of Recombinant Mouse Endostatin from E. coli under Experimental Procedures for the fusion protein comprising endostatin linked to His tag and protein kinase A recognition sequence, composition comprising said endostatin and pharmaceutically acceptable carrier at Treatment of Murine Primary Malignant Tumors

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under Experimental Procedures. O'Reilly et al teach that the 20 kDa C-terminal fragment of collagen XVIII (aka, endostatin) inhibits angiogenesis. Note Fig. 6C for example. O'Reilly et al refers Oh et al at page 278 left column, line 5 of second paragraph for the sequence information about the endostatin shown at Fig. 2B. Thus O'Reilly et al anticipate instant claims 2-4, 11, and 13-15.

Claims 2-4, 12-16, and 35 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat 5,854,205 (IDS AA, O'Reilly et al) as evidenced by Oh et al (1994, a copy provided with the Office action, Paper No. 9, Proc. Natl. Sci. Acad. USA., vol. 91, pages 4229-33) for the C-terminal 20 kDa fragment sequence information of the collagen type XVIII.

The rejection is based on the Office's interpretation that the limitation "comprising" in line 1 of the base claim controls the scope of the claims 2-4, and 12-16. See the rejection under 102 (a) above. Note the '205 patent is based on O'Reilly et al reference cited in 102 (a) rejection above. The '205 patent does not list the instant sequence. However, the patent refers to Oh et al (see for example column 22 line 16) and others for the exact amino acid composition. The '205 patent teaches endostatin protein with anti-angiogenic activity, composition comprising endostatin and angiostatin and others (note abstract, Fig. 8 C, 12C, claims 1-34). The broadly drawn claim 1 of the '205 patent encompasses the vague instant claim 35 because the instant specification in the paragraph bridging page 15-16 says that anti-angiogenic activity includes cessation (interpreted as inhibition) of endothelial cell proliferation. Note also applicant's stated position on what constitutes "anti-angiogenic activity" at page 7 line



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21-22 of Paper No. 11. Thus US Pat 5,854,205 anticipates instant claims 2-4, 12-16, and 35.

Claim 35 is rejected under 35 U.S.C. **102(e)** as being anticipated by US Pat 6,080,728 (filed Dec. 5, 1997).

This rejection is based on the definition of "mutant" of EM1 in the paragraph bridging at page 17-18. The claim as written read on SEQ ID NO:36 of the '728 patent (a endostatin peptide) with 94.6 % identity to instant SEQ ID NO:2. The patent teaches that said endostatin peptide is a anti-angiogenic protein. Note claims 1 and 6, also note column 7 of the '728 patent. Thus the patent anticipates instant claim 35.

#### ***Allowable Subject Matter***

A protein consisting of amino acid number 1-175 of SEQ ID NO:2 is free of art and the specification shows that said protein has anti-angiogenic activity.

#### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

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305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu  
June 23, 2003

  
ANTHONY C. CAPUTA  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

Db 12 HTHDDFQVHLVALNTPLSGMRGIRGADFCFOQARAVGLSCPRALFSSRLDLYSI 71  
QY 61 VRRADRGSPVIVNKKDEVLSPSNDLSFGSGOQLOPGARIFSFQGRDYLRRHPAMPQKSV 120  
Db 72 VRRADRGSPVIVNKKDEVLSPSNDLSFGSGOQLOPGARIFSFQGRDYLRRHPAMPQKSV 131  
QY 121 HGSDPSGRRLMESYCETWRTETTGATGQASSLSGRLLRLEOKAASCHNSYIVLCIENSFMT 180  
Db 132 HGSDPSGRRLMESYCETWRTETTGATGQASSLSGRLLRLEOKAASCHNSYIVLCIENSFMT 191  
QY 181 TSFSK 184  
Db 192 TSFSK 195

## RESULT 2

US-08-985-526-36  
Sequence 36 Application US/08985526  
Patent No. 6080728

## GENERAL INFORMATION:

APPLICANT: Mixson, James A  
TITLE OF INVENTION: CARRIER:DNA COMPLEXES CONTAINING DNA  
TITLE OF INVENTION: ENCODING ANTI-ANGIOGENIC PEPTIDES AND THEIR USE IN GENE  
TITLE OF INVENTION: THERAPY  
NUMBER OF SEQUENCES: 43  
CORRESPONDENCE ADDRESSES:  
ADDRESSEE: Connolly, Bove, Lodge, & Butz  
STREET: 1220 Market Street, P.O. Box 2207  
CITY: Wilmington  
STATE: Delaware  
COUNTRY: U.S.A.  
ZIP: 19899

## COMPUTER READABLE FORM:

MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: Patentin Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/985,526  
FILING DATE:

## CLASSIFICATION:

Prior Application DATA:

APPLICATION NUMBER: US 08/608,845  
FILING DATE: 16-JUL-1996

ATTORNEY/AGENT INFORMATION:

NAME: McMorrow Jr., Robert G  
TELECOMMUNICATION INFORMATION:

TELEPHONE: (302) 658-9141  
TELEFAX: (302) 658-5613

INFORMATION FOR SEQ ID NO: 36: ✓

SEQUENCE CHARACTERISTICS:

LENGTH: 185 amino acids  
TYPE: amino acid  
TOPOLOGY: linear

US-08-985-526-36

## Query Match

Best Local Similarity 94.6%; Score 916; DB 3; Length 185;  
Matches 176; Conservative 5; Mismatches 2; Indels 2; Gaps 2;

QY 1 HTHDDFQVHLVALNTPLSGMRGIRGADFCFOQARAVGLSCPRALFSSRLDLYSI 60  
Db 2 HTHDDFQVHLVALNTPLSGMRGIRGADFCFOQARAVGLSCPRALFSSRLDLYSI 60  
QY 61 VRRADRGSPVIVNKKDEVLSPSNDLSFGSGOQLOPGARIFSFQGRDYLRRHPAMPQKSV 119  
Db 61 VRRADRGSPVIVNKKDEVLSPSNDLSFGSGOQLOPGARIFSFQGRDYLRRHPAMPQKSV 120  
QY 120 HGSDPSGRRLMESYCETWRTETTGATGQASSLSGRLLRLEOKAASCHNSYIVLCIENSFMT 179  
Db 121 HGSDPSGRRLMESYCETWRTETTGATGQASSLSGRLLRLEOKAASCHNSYIVLCIENSFMT 180

QY 180 TSFSK 184  
Db 181 TSFSK 185

## RESULT 3

US-09-206-059-2  
Sequence 2 Application US/09206059  
Patent No. 6201104

## GENERAL INFORMATION:

APPLICANT: Macdonald, Nicholas  
APPLICANT: Sim, Kim Lee

TITLE OF INVENTION: Angiogenesis-Inhibiting Protein Binding Peptides and

FILE REFERENCE: 05213-0370  
CURRENT APPLICATION NUMBER: US/09/206,059  
CURRENT FILING DATE: 1998-12-04

NUMBER OF SEQ ID NOS: 80  
SOFTWARE: Patentin Ver. 2.0

SEQ ID NO: 2

LENGTH: 183

TYPE: PRT

ORGANISM: Homo sapiens

US-09-206-059-2

## Query Match

Best Local Similarity 86.8%; Score 840; DB 4; Length 183;  
Matches 155; Conservative 15; Mismatches 11; Indels 0; Gaps 0;

QY 1 HTHDDFQVHLVALNTPLSGMRGIRGADFCFOQARAVGLSCPRALFSSRLDLYSI 60  
Db 1 HSHDDFQVHLVALNTPLSGMRGIRGADFCFOQARAVGLSCPRALFSSRLDLYSI 60

QY 61 VRRADRGSPVIVNKKDEVLSPSNDLSFGSGOQLOPGARIFSFQGRDYLRRHPAMPQKSV 120  
Db 61 VRRADRGSPVIVNKKDEVLSPSNDLSFGSGOQLOPGARIFSFQGRDYLRRHPAMPQKSV 120

QY 121 HGSDPSGRRLMESYCETWRTETTGATGQASSLSGRLLRLEOKAASCHNSYIVLCIENSFMT 180  
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QY 181 S 181  
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